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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/660,862	09/13/2000	William Pollack	ATOPH:52516	7947

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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	12

DATE MAILED: 05/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/660,862	POLLACK, WILLIAM	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Office Action is responsive to Applicant's response in paper No. 10 to Office Action in paper No. 8. In response to the Amendment filed February 26, 2002, claims 10-13 have been cancelled. Applicant's Declaration under 37 C.F.R. 1.132 is acknowledged. Claims 1 and 5-9 are pending and under consideration.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

3. In view of Applicant's amendment the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

4. Applicant's amendment and Declaration under 37 C.F.R. 1.132 filed February 26, 2002 are sufficient to overcome the following Rejections and the rejections have been withdrawn:

a) Rejection of claim 5 under 35 U.S.C. 112, second paragraph, page 4, paragraph 5 of previous Office action.
b) Rejection of claim 1 under U.S.C. 102(b), pages 4-5, paragraph 6, of the previous Office action.
c) Rejection of claims 1 and 5 under 35 U.S.C. 103(a), pages 6-7, paragraph 7 of the previous Office action.
d) Rejection of claims 1 and 6-7 under 35 U.S.C. 103(a), pages 7-8, paragraph 8 of the previous Office action.
e) Rejection of claims 1 and 8-9 under 35 U.S.C. 103(a), pages 9-10, paragraph 9 of the previous Office action.

5. The rejection of claim 1 under U.S.C. 112, first paragraph is maintained for reasons set forth in paper 8, pages 3-4, paragraph 4 of the previous Office Action.

The rejection was on the grounds that Claim 1 is rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "essentially free". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "essentially free" cannot be ascertained. Clarification as to the meaning of this term is required.

Applicant urges that "essentially free" refers to other IgG subtypes other than IgG4. The Applicant refers to the specification, page 7, lines 26-27 for clarification of "essentially free", which states " this effluent is mostly, if not entirely, IgG4". It is the Examiner's position that there is nothing on the record that defines "mostly". Therefore, it is unclear as to what the Applicant is referring? Therefore, the metes and bounds of "essentially free" cannot be ascertained.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 6 and 7 contains the trademark/trade names DEAE Sepharose® and CM-Sepharose®, respectively. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the

trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe anion and cation exchange resins and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 1 is rejected under 35 U.S.C. 35 U.S.C. 103(a) as being unpatentable over Bird et al *(Journal of Immunological Methods, 71, 1984, 97-105)*.

Claim 1 is drawn to a method of manufacturing IgG_4 immune globulin that comprises the steps of: (a) adjusting plasma to a pH of about 6.5 and a conductivity of between 3.5 to 6 millisiemens, (b) contacting the plasma obtained from step (a) with an anion exchange resin to obtain an anion exchange effluent and (c) contacting the effluent of step (b) with an anion exchange resin to obtain a cation exchange effluent that comprises IgG4 essentially free of other IgG subtypes.

Bird et al teach a method of separating human serum IgG into subclass fractions which includes IgG4 by immunoaffinity chromatography (see the Title and page 98). Bird et al teach the use of Sepharose columns and DEAE columns (page 98). Bird et al teach that the pH for affinity purifications ~~were~~ was pH 4-8 for all IgG subclasses (Figure 1, page 100).

The recitation of "conductivity of between 3.5 to 6 millisiemens" would be an obvious experimental design choice since adjusting conductivity is well known by those ~~that~~ who are skilled in the art.

8. Claims 1 and 5-9 are rejected under 35 U.S.C. 35 U.S.C. 103(a) as being unpatentable over Bird et al *(Journal of Immunological Methods, 71, 1984, 97-105)* in view of Laursen et al *(US Patent No. 6,281,336, published August 23, 2001).*

Claims 1 and 5-9 are drawn to a method of manufacturing IgG$_4$ immune globulin that comprises the steps of: (a) adjusting plasma to a pH of about 6.5 and a conductivity of between 3.5 to 6 millisiemens, (b) contacting the plasma obtained from step (a) with an anion exchange resin to obtain an anion exchange effluent and (c) contacting the effluent of step (b) with an anion exchange resin to obtain a cation exchange effluent that comprises IgG4 essentially free of other IgG subtypes.

Bird et al teach a method of separating human serum IgG into subclass fractions which includes IgG4 by immunoaffinity chromatography and the use of Sepharose columns and DEAE columns (see the Title and page 98). Bird et al teach that IgG ~~were~~ was prepared from human serum immunoglobulin. Bird teach that a stepwise fractionation

on DEAE columns using sodium phosphate. Bird et al teach that a buffer containing NaCl was used to wash the Sepharose column. Bird et al teach that citric acid was added until a desired pH was achieved. Bird et al teach ~~Bird et al teach~~ that the pH for affinity purifications ~~were~~ was pH 4-8 for all IgG subclasses (Figure 1, page 100). Bird et al teach that for the production of IgG subclasses negative affinity columns were used and that IgG4 coupled with a positive affinity column "concentration step was used (page 102).

Bird et al do not teach the use of exchange resins DEAE Sepharose® and CM-Sepharose®.

Laursen et al teach a method of producing immunoglobulins and other immunoglobulin products (see the Title). Laursen et al teach the use of DEAE Sepharose® and CM-Sepharose® exchange resins in the method of producing immunoglobulin and immunoglobulin products (column 7). Laursen et al teach a method of producing immunoglobulins by starting with normal human plasma or plasma from donor with high titers of specific antibodies (i.e. hyperimmune plasma) (column 4). Laursen et al teach that the method for producing IgG immunoglobulins and immunoglobulin products include: 1) purification of the Cohn fraction by preparing Cohn fraction from human plasma by adjusting the pH, ethanol concentration, adjusting temperature and protein concentration, 2) extraction of the immunoglobulin from the Cohn extraction by adding sodium phosphate, adjusting pH, filtering, centrifuging and re-filtering the suspension and 3) purification of by serial anion and cation exchange chromatography using DEAE Sepharose® and CM-Sepharose® resins. Laursen et al teach that the IgG is eluted with a gradient of NaCl when the CM-Sepharose column is

used (column 15-16). Laursen et al teach the addition of saccharides to the IgG fraction to stabilize the IgG fraction (column 9, lines 17-26 and column 4, lines 20-23). Lactose, is a saccharide which is well known in the art as being a protein stabilizer. It is well known in the art to freeze and later thaw purified fractions at certain convenient points in the process of antibody purification. This is done to pool large amounts of purified antibody fractions before use or further processing or to store purified antibody fractions to be used at a later date. This is evidenced by Rhodes *(U.S. Patent No. 5,346, 687, published September 13, 1994)* ~~which~~ who teaches that frozen purified antibody can be frozen in a vial and maintained for indefinite period before use (claim 5). It is also well known in the art to lyophilize immunoglobulins to store them to be used at a later date.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use exchange resins DEAE Sepharose® and CM-Sepharose® as taught by Laursen et al in the method of separating human serum IgG into subclass fractions which includes IgG4 by immunoaffinity chromatography as taught by Bird et al because Bird et al teach to obtain a purified IgG4 preparation a second run on appropriate affinity columns may be necessary (pages 97-98) and Laursen et al teach that the use of DEAE Sepharose® and CM-Sepharose® exchange resins connected in series would provide a high degree of purity and high content of IgG monomers and dimers which is partly due to the use of two serially connected chromatography columns (column 7, lines 20-26). It would have been expected barring evidence to the contrary, that the use of DEAE Sepharose® and CM-Sepharose®

exchange resins connected in series would have the advantages making the operation more practical and there is no need for an intermediary step of collecting the IgG-containing fraction between ion exchange chromatographic methods for possible adjusting pH and ionic strength (column 7, lines 8-20).

Pertinent Prior Art

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Persson, Journal of Immunological Methods, 98, 91-19 and Lambin et al, Journal of Immunological Methods, 165, 1993, p. 99-111).*

Status of Claims

10. No claims are allowed.

LYNETTE R. F SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 16

Conclusion

11. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
April 30, 2002

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SUPERVISORY PATENT EXAMINER
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